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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/485,896	06/01/2000	WOLFGANG PIEPERSBERG	RDID0011US	6502

7590 11/15/2001

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EXAMINER

STEADMAN, DAVID J

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 11/15/2001

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/485,896

Applicant(s)

PIEPERSBERG ET AL.

Examiner

David J. Steadman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 14-35 is/are pending in the application.
- 4a) Of the above claim(s) 15-17, 26-30 and 32-34 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☐ Claim(s) 14, 18-25, 31 and 35 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

Status of the Application

Claims 14-35 are pending in the application.

Applicants election without traverse of Group I, claims 14, 18-25, 31, and 35, drawn to a process for the production of guanosine diphosphate (GDP)-D-mannose using phosphomannomutase (ManB) and GDP-D-mannose synthase (ManC) enzymes in Paper No. 9, filed 06 September, 2001 is acknowledged.

Claims 15-17, 26-30, and 32-34 and the subject matter of Groups II-IV as set forth in Paper No. 8 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim.

Drawings

1. The drawings submitted with this application are objected to by the Draftsperson. Refer to the attached "Notice of Draftsperson's Patent Drawing Review" for details. Direct any inquiries concerning drawing review to the Drawing Review Branch (703) 305-8404.

Specification/Informalities

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "PROCESS FOR THE PRODUCTION OF GDP-D-MANNOSE USING PHOSPHOMANNOMUTASE AND GDP-D-MANNOSE SYNTHASE ENZYMES". See MPEP § 606.01.

3. It is suggested that "Legends for the figures" at the middle of page 8 of the specification be replaced with, for example, "Brief Description of the Drawings".

Claim Objections

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4. Claims 14 and 20 are objected to because the claims are drawn to non-elected subject matter. It is suggested that, for example, applicants amend the claims accordingly to remove non-elected subject matter from the claims.

5. Claim 21 is objected to because of the recitation of "E. coli" and "Corynebacterium sp.". Abbreviations should not be recited in the claims without at least once reciting the entire phrase, i.e., "Escherichia coli" and "Corynebacterium species" for which the abbreviation is used. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 14, 18-25, and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claims 14 (claims 21, 23, and 24 dependent therefrom), 18-20, 22, 25 are confusing in that it is not clear whether the process uses a single polypeptide encoded from a single polynucleotide having multiple enzymatic activities as set forth in claims 14 and 22, or if the claim is to be interpreted as a process using multiple polypeptides encoded by multiple polynucleotides. The examiner has interpreted the claims as a plurality of polypeptides encoded by a plurality of polynucleotides. If the examiner's interpretation of these claims is incorrect, applicant should so state and clarify the record.

8. Claim 35 is indefinite for depending upon non-elected claims 32-34. It is suggested that, for example, applicants replace the term "claims 31-34" with "claim 31".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which

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it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 14, 18-21, and 23-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process for the production of GDP-D-mannose using phosphomannomutase (ManB) and GDP-D-mannose synthase (ManC) enzymes with GTP and D-mannose-6-phosphate as starting materials, does not reasonably provide enablement for a process for the production of any GDP-6-deoxyhexose using phosphomannomutase (ManB) and GDP-D-mannose synthase (ManC) enzymes with a starting substance selected from GDP-D-mannose, precursors, and secondary products thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claim 14 (claims 18-21 and 23-25 dependent therefrom) are so broad as to encompass a process for the production of any GDP-6-deoxyhexose using phosphomannomutase (ManB) and GDP-D-mannose synthase (ManC) enzymes with a starting substance selected from GDP-D-mannose, precursors, and secondary products thereof. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of GDP-6-deoxyhexoses and precursors and secondary products of GDP-D-mannose broadly encompassed by the claims. In this case the disclosure is limited to a process for the production of GDP-D-mannose using phosphomannomutase (ManB) and GDP-D-mannose synthase (ManC) enzymes with GTP and D-mannose-6-phosphate as starting materials.

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The specification does not support the broad scope of the claims which encompass a process for the production of any GDP-6-deoxyhexose using phosphomannomutase (ManB) and GDP-D-mannose synthase (ManC) enzymes with a starting substance selected from GDP-D-mannose, precursors, and secondary products thereof because the specification does not establish: (A) a method for producing GDP-6-deoxyhexose using *any* precursors and secondary products of GDP-D-mannose using ManB and ManC as catalysts because it appears from Fig. 1 that enzymes in addition to ManB and ManC are required for GDP-6-deoxyhexose synthesis and in the event that ManB and ManC enzymes are sufficient for GDP-6-deoxyhexose synthesis, it is unclear that these enzymes will have specificity for *any* precursors and secondary products of GDP-D-mannose; (B) the general tolerance of the method to modification and extent of such tolerance; and (C) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a process for the production of any GDP-6-deoxyhexose using phosphomannomutase (ManB) and GDP-D-mannose synthase (ManC) enzymes with a starting substance selected from GDP-D-mannose, precursors, and secondary products thereof. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 14, 18-23, and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Elling et al. (Glycobiology 6:591-7). Claims 14, 18-23, and 31 are drawn to processes for the biosynthetic production of GDP-6-deoxyhexose or GDP-D-mannose using ManB and ManC enzymes as encompassed by the claims.

Elling et al. teach amplification of *Salmonella enterica* rfbK and rfbM genes encoding phosphomannomutase (EC 5.4.2.8) and GDP- α -D-mannose pyrophosphorylase (EC 2.7.7.13), respectively, cloning of said amplified genes into expression vectors, transforming *E. coli* with said vectors, expression of said enzymes (pages 591-2, under *Expression of phosphomannomutase and GDP- α -D-mannose pyrophosphorylase*), purification of said enzymes (pages 592, under *Enzyme purification*), and the use of said enzymes in the presence of D-mannose-6-phosphate and GTP (page 592, Fig. 1) for the batchwise production of GDP- α -D-mannose and isolation of the GDP- α -D-mannose by chromatographic and precipitation steps (page 592, under *Preparative synthesis and isolation of GDP- α -D-mannose*). This anticipates claims 14, 18-23, and 31 as written.

It is noted that applicants disclose in the specification at pages 2, 5, and 6 that phosphomannomutase is otherwise known as ManB and is encoded by the manB gene and GDP-mannose pyrophosphorylase is otherwise known as GDP-mannose synthase or ManC and is encoded by the manC gene. Therefore, the products of the rfbK and rfbM genes, i.e., phosphomannomutase and GDP- α -D-mannose pyrophosphorylase, respectively, are inherently the same as the ManB and ManC enzymes, respectively.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the

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subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. Claims 24, 25, and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elling et al. in view of US Patent 5,071,750 ('750). Claims 24, 25, and 35 are drawn to a process for the biosynthetic production of GDP-6-deoxyhexose or GDP-D-mannose using cloned ManB and ManC enzymes, wherein: 1) the process is carried out continuously in an enzyme-membrane reactor (EMR) as encompassed by claim 24, 2) the enzyme is immobilized to a solid support and a buffer containing the substrates is percolated thereover (claim 25), or 3) the enzyme is immobilized on a solid support (claim 35).

Elling et al. disclose the teachings described above.

'750 teaches the use of immobilized enzymes covalently coupled to a solid support for continuous enzymatic production of product. '750 also teaches the use of an EMR for continuous enzymatic biosynthesis, wherein the enzymes are retained by an ultrafiltration membrane which is located in front of the reactor outlet having an appropriate cut-off (column 3, lines 54-60). '750 teaches that the advantage of using immobilized enzymes or EMR for biosynthesis is the facilitation of product isolation (column 4, lines 1 and 2).

Therefore, it would have been obvious to one of ordinary skill in the art to practice the method of Elling et al. using immobilized enzymes or an EMR as taught by '750 for the biosynthetic production of GDP-D-mannose. One would have been motivated to practice the method of Elling et al. using immobilized enzymes or an EMR as taught by '750 for the biosynthetic production of GDP-D-mannose because of the teachings of '750 as described above. One would have a reasonable expectation of success for practice the method of Elling et al. using immobilized enzymes or an EMR as taught by '750 for the biosynthetic production of GDP-D-mannose because of the results of Elling et al. and '750. Therefore, claims 24, 25, and 35, drawn to a process for the biosynthetic production of GDP-6-deoxyhexose or GDP-D-mannose using cloned ManB and ManC enzymes, wherein: 1) the process is carried out continuously in an enzyme-membrane reactor (EMR) as encompassed by claim 24, 2) the

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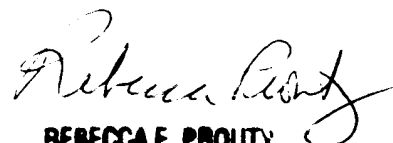
enzyme is immobilized to a solid support and a buffer containing the substrates is percolated thereover (claim 25), or 3) the enzyme is immobilized on a solid support (claim 35) would have been obvious to one of ordinary skill in the art.

Conclusion

12. No claim is in condition for allowance. All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Friday from 7:30 am to 2:00 pm and from 3:30 pm to 5:30 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for this Group is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.


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